Harmine inhibits breast cancer cell migration and invasion by inducing the degradation of Twist1.

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Public Summary:
Breast cancer is the leading cause of cancer-related deaths in the United States. The majority of deaths (90%) in breast cancer patients is caused by invasion and metastasis-two features related to the epithelial-to-mesenchymal transition (EMT). Twist1 is a key transcription factor that promotes the EMT, which leads to cell migration, invasion, cancer metastasis, and therapeutic resistance. Harmine is a beta-carboline alkaloid found in a variety of plants and was recently shown to be able to induce degradation of Twist Family BHLH Transcription Factor 1 (Twist1) in non-small cell lung cancer cells (NSCLC). In this study, we show that harmine can inhibit migration and invasion of both human and mouse breast cancer cells in a dose-dependent manner. Further study shows that this inhibition is most likely achieved by inducing a proteasome-dependent Twist1 degradation. At the concentrations tested, harmine did not affect the viability of cells significantly, suggesting that its inhibition of cancer cell migration and invasion is largely independent of its cytotoxicity, but due to its ability to affect regulators of EMT such as Twist1. This result may facilitate the development of strategies that target Twist1 to treat metastatic breast cancer, as Twist1 is expressed at a high level in metastatic breast cancer cells but not in normal cells.

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